ABSTRACTS

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Growth rate and associated factors in small abdominal aortic aneurysms

Vega de Ceniga M, Gomez R, Estallo L, et al. Eur J Vasc Endovasc Surg 2006;31:231-6

Conclusion: Growth rates of small abdominal aortic aneurysms (AAAs) increase with the baseline size of the aneurysm. Both diabetes and chronic limb ischemia reduce growth rate of small AAAs.

Summary: This was a longitudinal, observational, prospective study to evaluate growth rates of small AAAs and factors that may influence growth. Patients with AAAs <5 cm in diameter were divided into two groups by a baseline ultrasound examination. Group I patients had aneurysms between 3 and 3.9 cm (n = 246), and group II patients had aneurysms between 4 and 4.9 cm (n = 106). Patients in group I underwent annual ultrasound scans, and patients in group II underwent CT scans every 6 months. There were 352 patients (333 men and 19 women) monitored for a mean of 55.2 ± 37.4 months (range, 6.3 to 199.8 months).

Aneurysm growth rate was greater in patients in group II (4.72 ± 5.93 mm/y vs 2.07 ± 3.23 mm/y; $P < 0.0001$). During follow-up, 87 patients (24.7%) died. One patient died because of a ruptured AAA and one died during elective aneurysm repair. Two aneurysms ruptured in group II: one had expanded to 5.6 cm, and the second had expanded to 6 cm. Rapid expansion (defined as >4 mm/y) was more prevalent in group II than group I (36.8% vs 13.8%; $P < .0001$). No expansion (0 mm) was observed in 17.9% of patients in group II and 25.2% of patients in group I ($P = .14$). During the follow-up period there were 36 patients (14.6%) in group I where the aneurysm grew to 5 cm in diameter, and there were 72 patients (67.9%) in group II where the aneurysm reached 5 cm in diameter (odds ratio 12.35; 95% confidence interval, 7.19 to 21.28; $P < .0001$).

Cardiovascular risk factors did not influence growth rate in group I. Diabetic patients in group II had significantly lower growth rates than nondiabetic patients (1.69 ± 3.51 vs 5.22 ± 6.11 mm/y; $P = .032$). Chronic limb ischemia was associated with slower aneurysm expansion (odds ratio 0.47; 95% confidence interval, 0.22 to 0.99; $P = .045$).

Comment: There are no major surprises here. Small aneurysms rupture very infrequently, and larger small aneurysms grow faster than smaller small aneurysms. The differential affects of cardiovascular risk factors on growth rate of aneurysms, although previously shown, is perhaps not as well appreciated. The UK Small Aneurysm Trial also demonstrated decreased growth rates of aneurysms in patients with peripheral arterial disease and in patients with diabetes (Circulation 2004;110:16-21). Observations with respect to peripheral arterial disease and diabetes on growth rate of small AAAs observed in this study are therefore unlikely the result of chance. There may be changes in the collagen vs elastin content of the aortic wall in patients with diabetes or in those whose atherosclerotic risk factors have produced both occlusive as well as aneurysmal disease.

Effect of very high-intensity statin therapy on regression of coronary atherosclerosis: the ASTEROID trial

Missen FE, Nicholls SJ, Sipahi I, et al, and the ASTEROID Investigators. JAMA 2006;295:1556-65

Conclusion: Very-high-intensity statin therapy with rosuvastatin can reduce coronary atherosclerosis as assessed by intravascular ultrasound (IVUS).

Summary: The authors performed a prospective, open-labeled, blinded end point trial to determine the effect of very-high-intensity statin therapy on coronary atherosclerosis as assessed by IVUS. The study was conducted in 53 community and tertiary medical centers in the United States, Canada, Europe, and Australia. Coronary atheromas were assessed at baseline and after 24 months of treatment. A total of 507 patients had a baseline IVUS examination and received at least one 40-mg dose of rosuvastatin a day. There was no placebo arm of the trial, with all patients receiving 40 mg/d of rosuvastatin. At 24 months, 349 patients had an evaluable IVUS examination. Primary efficacy parameters were a change in atheroma volume percentage measured by IVUS and change in atheroma volume in a 10-mm subsegment of artery with the greatest disease severity at baseline. A second efficacy variable was normalized atheroma volume for the entire artery.

At baseline, the mean low-density lipoprotein cholesterol (LDL) was 130.4 ± 34.3 mg/dL. This declined to 60.8 ± 20.0 mg/dL with treatment with rosuvastatin, a mean reduction of 53.2% ($P < .001$). The mean high-density lipoprotein cholesterol (HDL) level at baseline was 43.1 ± 11.1 mg/dL. This increased to 49.0 ± 12.6 mg/dL with rosuvastatin treatment, an increase of 14.7% ($P < .001$). The mean change in the percentage of atheroma volume was −0.98% ± 3.15% with a median of −0.79% (97.5% confidence interval [CI], −1.21% to −0.53%), $P < .001$ compared with baseline. The mean change in atheroma volume in the most diseased 10-mm subsegment was −6.1 ± 10.1 mm^3, with a median change of −5.6 mm^3 (97.5% CI, −6.8 mm to −.40 mm^3), $P < .001$ compared with baseline. Total atheroma volume showed a 6.8% median reduction, with a mean reduction of −14.7 ± 25.7 mm^3 and a median reduction of −12.5 mm^3 (95% CI, −15.5 to 10.5 mm^3), $P < .001$ compared with baseline.

Comment: This study demonstrates convincing regression of atherosclerosis in the coronary circulation with high-dose statin therapy. The study has some limitations in that there was no placebo control. Also, 22 patients were withdrawn because of ischemic events, and those patients may represent actual progression of atherosclerosis under the treatment protocol. Nevertheless, in the patients evaluated, coronary atherosclerosis was reduced with the high-dose statin therapy used in this study. There were minimal complications and intolerance associated with the drug. It seems clear that high-dose statin therapy is indicated for patients with significant coronary disease. There is no evidence to date, however, that such therapy will benefit patients with cerebrovascular or peripheral arterial disease. Those trials still need to be done.

Improvement in stroke mortality in Canada and the United States, 1990–2002

Quanhe Y, Botto L, Erickson JD, et al. Circulation 2006;113:1343-53

Conclusion: Stroke mortality has improved in the United States and Canada during the period of folic acid fortification of grain products. This suggests high homocysteine levels are independent risk factors for stroke and can be modified by folic acid fortification of grain products.

Summary: Folic acid fortification of grain products was fully implemented in the United States and Canada by 1998. Theoretically, this should result in a population-wide reduction in blood homocysteine levels. If it is assumed high homocysteine levels are an independent risk factor for stroke, this should result in a decrease in stroke mortality. The authors sought to address the hypothesis fortification of grain products with folic acid reduces stroke mortality in the United States and Canada. They used segmented log-linear regression analysis to evaluate stroke mortality trends before and after folic acid fortification of grain products. These data were compared with stroke mortality during the same period in England and Wales, where fortification of grain products with folic acid was not required.

Average blood homocysteine concentrations decreased and average blood folate concentrations increased in the United States after fortification. The previously observed decline in stroke mortality in the United States from 1990 to 1997 further accelerated from 1998 to 2002 in virtually all segments of the population. Overall, change varied from −0.3% (95% confidence interval [CI], −0.7 to 0.08) to −2.9 (95% CI, −3.5 to −2.3) per year ($P = .0005$). Sensitivity analysis indicated there were no other major recognized risk factor changes to account for the decreased trend of stroke-related deaths in the United States. In Canada, the fall in stroke mortality averaged −1.0% (95% CI, −1.4 to −0.6) per year from 1990 to 1997. This accelerated to −5.4% (95% CI, −6.0 to −4.7) per year from 1998 to 2002 ($P \leq .0001$). There was no change in stroke mortality in England and Wales from 1990 to 2002.

Comment: These data provide indirect evidence that stroke mortality can be modified by reducing overall homocysteine levels in the population. The sophisticated statistical methods used in this report make it unlikely that the findings presented represent chance alone. It is, however, unknown whether the reduction in stroke mortality is secondary to a decrease incidence of stroke or a decrease in the case fatality rate of stroke, and thus reflecting better stroke care rather than decreased stroke incidence.

Matrix metalloproteinase-8 and -9 are increased at the site of abdominal aortic aneurysm rupture

Wilson WRW, Anderton M, Schwalbe EC, et al. Circulation 2006;113:438-45

Conclusion: There is an increase of matrix metalloproteinase-8 (MMP-8) and MMP-9 at the site of aortic aneurysm rupture.

Summary: Processes that lead directly to abdominal aortic aneurysm (AAA) rupture are not well understood. The authors sought to study the role of MMPs and their inhibitors (TIMPs) in the cellular and proteolytic activity of ruptured AAAs. Biopsy specimens were obtained from the anterior wall of the aorta from 20 ruptured and 55 nonruptured AAAs. In 12 of the ruptured AAAs, biopsy specimens were taken from rupture site and analyzed for MMP-1, -2, -3, -8, -9, and -13. TIMP-1 and TIMP-2 were all